from both ExpF-based treatments were almost identical.

Not all xylem-mobile molecules behave in the same way and this is illustrated by a comparison between ExpF and fluquinconazole when both were mixed with Adj1. Fluquinconazole was recovered only in very small quantities, the single greatest recovery being 0.17% over a 24h period. These recoveries are considerably less than those already described for ExpF when mixed with the same adjuvant. That recovery in guttation fluid is not solely related to the level of uptake into the plant is supported by data from other experiments (Harris RI unpublished) where the uptakes of both fluquinconazole and ExpF were very similar when mixed with Adj1 (60 and 69%, respectively, 24h after application).

Using ExpF as a model compound it should be possible to investigate the behaviour of other formulation systems on target crops. A specific example of the use of this system is the evaluation of encapsulated formulations. It is possible to prepare capsules with a range of properties, one of these being ease of capsule breakdown, resulting in the release of the encapsulated compound. This can be monitored using artificial surfaces, but there is now the possibility of doing studies *in vivo* using the model described above.

Information about the loss of fungicide, insecticide and herbicide molecules in guttation fluid can also help explain biological performance against target species. For example, the activity of ExpF against *Erysiphe graminis* DC f sp *tritici* Marchal, (the causal organism of powdery mildew of wheat) was enhanced when mixed with Adj2 but not Adj1 (Moss, N A pers. comm.). From the results discussed above it is possible that a biologically significant proportion of the applied dose of ExpF, when mixed with Adj1, was lost through guttation, resulting in an inferior performance compared with the mixture with Adj2. Life-cycle studies showed ExpF to be more effective as a protectant than curative fungicide and that the early stages of pathogen development were most affected. A formulation optimising surface retention rather than foliar uptake would, therefore, be more appropriate.

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Synthesis and insecticidal activity of 4-perhaloalkoxy (or thioalkyl) benzophenonehydrazone derivatives

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Abstract: Benzophenonehydrazone derivatives containing a mesylate or triflate substituent are known to exhibit insecticidal activity. In the present study, such substituents have been replaced by perhaloalkoxy groups. High levels of activity against lepidopteran pests were observed in greenhouse trials. For optimum activity, the substituents should be relatively small. In semi-field trials, however, none of the compounds tested showed sufficient persistence to warrant further development.

Keywords: benzophenonehydrazones; perhaloalkoxy substitution; insecticidal activity; lepidoptera; coleoptera; structure–activity relationships

1 INTRODUCTION

Amidinohydrazones have long been known for their pharmacological properties (eg for use against malaria).[1] Compounds of structure type **1** (Fig 1) were identified in the 1970s, as a class of insecticide active against lepidopteran and coleopteran pests.[2,3] Interest in this chemistry re-intensified in the 1990s. During our own investigations, we found that the triflate or mesylate substituent in **1** (Fig 1) could be replaced by a perhaloalkoxy substituent, whilst still preserving the biological activity. An optimisation programme was started to prepare compounds of structure type **2** (Fig 1) with the goal of improving the insecticidal properties and identifying compounds which could provide cost-effective control of lepidopteran and coleopteran pests in cotton and vegetables.[4]

The present communication gives an outline of the synthetical methodology used, together with selected biological data and structure–activity relationships.

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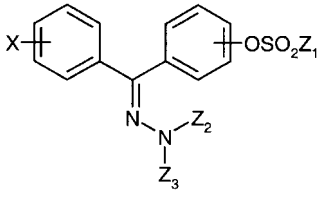

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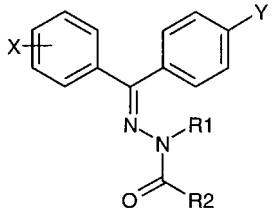

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X = 4-Cl, Br, F; R1 and R2 = H, alkyl, aryl
Y = OCF_3, OCF_2Br, OCF_2Cl, OCF_2CF_2Br, SCF_3

Figure 1. General structures of the compounds discussed in the text.

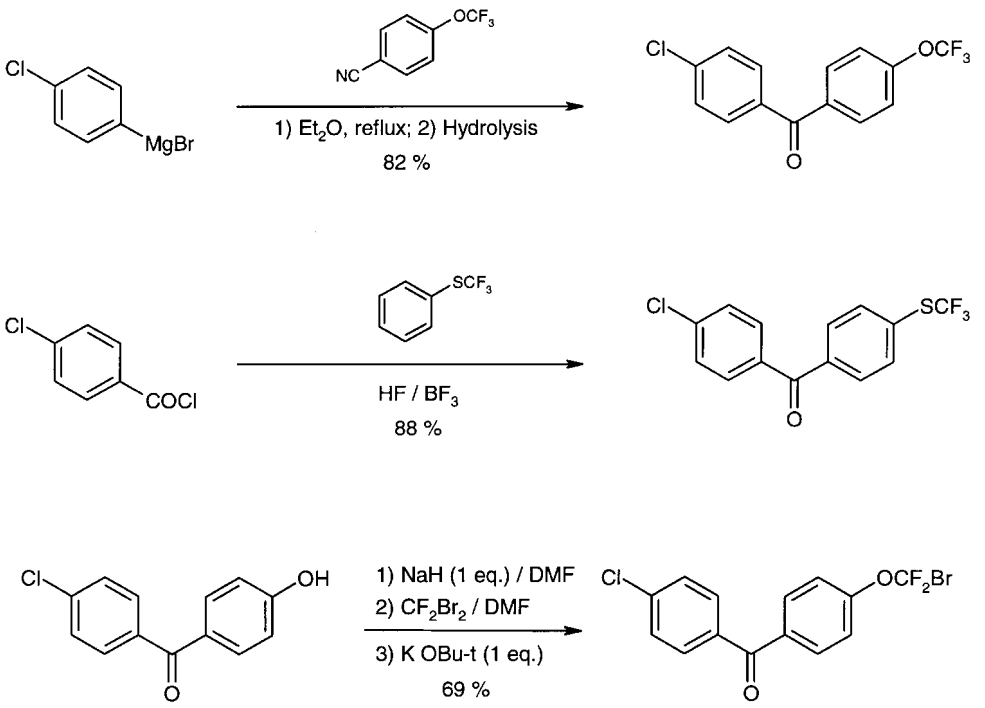

Figure 2. Examples of the preparation of the intermediate benzophenones.

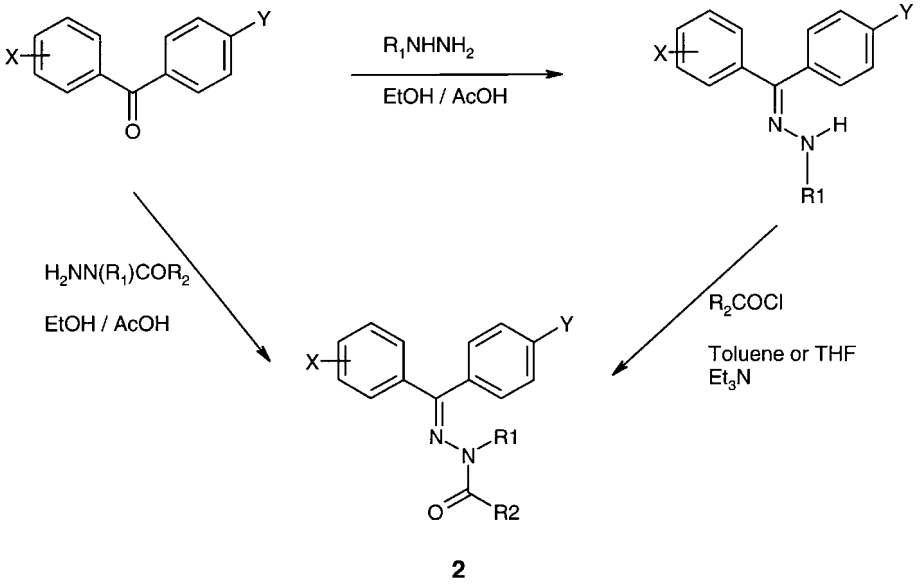

Figure 3. Synthesis of the final derivatives **2**.

2

2 EXPERIMENTAL METHODS

2.1 Synthetic methodology

2.1.1 General synthesis of intermediate benzophenones

Typical examples in Fig 2 include Friedel–Crafts and Grignard reactions, as well as alkylation of the corresponding phenols.

2.1.2 Preparation of the final products

The reaction of the benzophenone intermediates with a substituted hydrazine followed by acylation gives the desired compounds in fair to excellent yields. Alternatively, the benzophenone can be reacted directly with acylated hydrazines to yield the final derivatives **2**, as shown in Fig 3.

2.2 Insecticidal activity against chewing pests

Biological tests were performed in the glasshouse on the following lepidopteran and coleopteran pests: corn rootworm (*Diabrotica balteata* Lec), tobacco budworm (*Heliothis virescens* F, larval stages 1 and 3), diamondback moth (*Plutella xylostella* L.) and Egyptian leafworm (*Spodoptera littoralis* Boisd,) on maize seedlings or soya (cabbage) leaves.

3 RESULTS

The results in Tables 1 and 2 are indicated as ranges of approximated LD_{80} values in mg litre^{-1}; the substituents in the Tables are described according to the general formula **2** (Fig 1).

X^a	R_1[a]	R_2[a]	Activity[b] against[c] DIAB L2	HELI L1	HELI L3	PLUT L3	SPOD L3
4-Cl	H	CH_3	*****	*****	****	**	*****
		i-C_3H_7	****	****	****	****	****
	CH_3	H	*****	*****	****	****	****
		CH_3	*****	*****	****	****	****
	i-C_3H_7	H	*****	**	**	**	**
		CH_3	*****	****	**	****	****
		i-C_3H_7	****	*	*	**	*
4-Br	H	CH_3	*****	****	****	****	****
		i-C_3H_7	****	****	****	****	****
	CH_3	H	****	**	*	*	*
		CH_3	*****	****	**	**	**
		i-C_3H_7	**	**	*	**	*
4-F	H	CH_3	*****	****	**	**	****
Reference compound			*****	*****	****	****	*****

[a] See Fig 3.
[b] *Active at*: *****$\leq$3; **** 12; ** 25 to 50; * 100 mg litre^{-1}; - inactive, or active at $>$100 mg litre^{-1}.
[c] DIAB *Diabrolica balteata*; HELI *Heliothus virescens*; PLUT *Plutella xylostella*; SPOD Spodoptera littoralis; L1, L2, L3 larval stages.

Table 1. Biological activity of selected compounds with Y = OCF_2Br[a]

Table 2. Influence of the size of R_2 on biological activity. Selected examples with R1 = H, X = 4-Cl and Y = OCF_3[a]

R_2[a]	Activity[b] against[c] DIAB L2	HELI L1	HELI L3	PLUT L3	SPOD L3
CH_3 ***** [c]	****	****	****	**	
C_2H_5	****	**	**	**	**
c-C_3H_7	–	****	****	****	****
i-C_3H_7	–	**	**	**	****
n-C_3H_7	–	****	**	**	****
c-C_6H_{11}	–	**	*	*	*
C_6H_5	*	**	**	**	**

[a] See Fig 3.

The substitution pattern Y = OSO_2CF_3, X = 4-Cl, R_1 = H and R_2 = CH_3 was selected as the state of the art reference compound.[2] The results obtained with the analogue with Y = OCF_2Br (Table 1) are representative. Similar experiments were performed for other Y substituents (data not shown), the following being investigated: OCF_3, OCF_2Cl, SCF_3 and OCF_2CF_2Br.

3.1 Structure–activity relationships in the glasshouse

After the analysis of the available biological data, the following structure–activity relationships could be drawn:

Influence of the substituent Y: The order of activity was $OCF_2Br \geq OCF_3 = OCF_2Cl > SCF_3 \gg OCF_2CF_2Br$; the groups OCF_2Br, OCF_3 and OCF_2Cl gave rise to compounds showing good to excellent activity, whereas the other substituents led to inferior performance.

Influence of the substituents X: The chlorine atom was usually the best, the order being $Cl \geq Br > F$.

Influence of R_1 and R_2: The size of the substituent R_1 was critical, a group larger than methyl leading to a strong decrease of the activity: $H \geq CH_3 \gg$ i-C_3H_7.

For R_2, the same was true with *D balteata*. For the lepidopteran pests studied, the influence of R_2 was less clear. The results obtained with the series in Table 2 are typical. The range of substituents R_2 showing good biological performance against these pests seemed to be broader, up to C_3. Larger groups, including aromatics, were detrimental to the activity.

3.2 Further studies

A few of the best compounds in the above tests were selected for semi-field trials against *S littoralis* in Egypt, targeting the persistence on cotton under subtropical conditions. Unfortunately, none of the compounds tested showed sufficient persistence under those conditions.

4 CONCLUSIONS

The triflate or mesylate group could be effectively replaced by C_1-perhaloalkoxy groups. The activity level values of test compounds in the glasshouse were comparable to those of the reference compound. However, in semi-field trials, the compounds did not show good persistence against the Egyptian leafworm. The substitution patterns analysed in the present work did not lead to compounds which are likely to provide cost-effective control of lepidopteran pests in the field.

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Fate of famoxadone in the environment

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Abstract: The fate of famoxadone [Famoxate®, 3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione] in the aquatic and soil environment was examined. It was found to be relatively stable at pH 5, but hydrolysed rapidly in pH 7 and 9 buffer solutions. Primary hydrolytic degradation reactions included the opening of the oxazolidinedione ring and the cleavage of the oxazolidinedione-aminophenyl linkage. The compound degraded rapidly in soil by both hydrolytic and microbial action. In addition to the generation of [^{14}C] carbon dioxide and unextractable bound residues, hydroxylation and hydrolysis reactions occurred to yield multiple degradation products. Nitration of famoxadone at the 2- or 4-phenylamino position was observed as a novel non-biological degradation reaction of famoxadone in soil. Degradation in aqueous solution (pH 5) and on soil surfaces was accelerated under simulated sunlight irradiation. Famoxadone exhibited negligible soil mobility potential, and its primary degradation products were also shown to dissipate rapidly in the environment.

Keywords: famoxadone; hydrolysis; photolysis; soil; degradation

1 INTRODUCTION

Famoxadone [Famoxate®, DPX-JE874, 3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione; Fig 1,] is a novel fungicide being developed by DuPont Agricultural Products for the preventive control of a broad spectrum of fungal pathogens such as *Plasmopara viticola* Berl & de Toni (grape downy mildew), *Phytophthora infestans* (Mont) de Bary (potato/tomato late blight), *Pseudoperonospora cubensis* Rostow (cucumber downy mildew), *Septoria tritici* Rob (wheat leaf blotch), S *nodorum* Berk (wheat glume blotch) and *Alternaria solani* Sorauer (potato/tomato early blight). Excellent activity has been also observed against other Ascomycetes, as well as against pathogens within the *Pucciniaceae* family of the Basidiomycete class. Famoxadone has a novel mode of action in that it inhibits electron transport in oxidative phosphorylation in the fungal mitochondria and energy production.[1] It is highly active against spore germination and mycelial growth.[2] This summary describes the fate of famoxadone in water and soil test systems. Studies were conducted using famoxadone labeled in the phenoxyphenyl and in the phenylamino ring, abbreviated as [POP-^{14}C]- and [PA-^{14}C]famoxadone respectively (Fig 1).

2 EXPERIMENTAL AND RESULTS

2.1 Degradation in the aquatic environment

Famoxadone, with low water solubility (52 μg litre^{-1}), is relatively stable to hydrolytic degradation under dark conditions in pH5 buffer solution (half-life, DT_{50}:41 days) but hydrolyses rapidly in pH 7 and 9 buffer solutions at 25 °C (DT_{50} 2 days and <2 h, respectively). Primary hydrolytic degradation reactions include the opening of the oxazolidinedione ring *via* attack on either of the carbonyl moieties by hydroxide ion to yield compounds **2** and **3** (Fig 2), and the cleavage of the oxazolidinedione-aminophenyl linkage to yield various products from both the phenoxyphenyl (compounds **4** and **5**) and the aminophenyl moieties [benzene (**7**), catechol (**8**) and phenol (**9**)]. Famoxadone and its degradation products dissipate rapidly in the aqueous sediment system (DT_{50} < 1 day, DT_{90} 14 days). Significant impact or persistence in the aquatic environment is not anticipated. The hydrolysis pathway of famoxadone is presented in Fig 2.

Direct aqueous photolysis is not significant at pH 7; however, the degradation rate in acidic buffer solution (pH 5) is accelerated under simulated sunlight irradiation (DT_{50} 4.6 *vs* 41 days) to yield compounds **3, 4, 5, 8, 9** and **10**. Ring opening and cleavage of the oxazolidinedione-aminophenyl linkages are the primary reactions observed. Based on results from photodegradation studies with the parent and major degradation products compounds (**3, 4** and **10**), the profused aqueous photodegradation degradation pathway of famoxadone is presented in Fig 3.

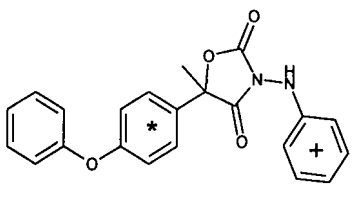

Figure 1. Structure of famoxadone. + Denotes [PA-^{14}C] famoxadone. *Denotes [POP-^{14}C] famoxadone.

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